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Changing livestock vaccination policy alters the epidemiology of human anthrax, Georgia, 2000–2013

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ABSTRACT

Anthrax is a widely spread zoonotic disease found on nearly every continent. To control the disease in humans and animals, annual livestock vaccination is recommended. However, in 2007, the country of Georgia ended its policy of compulsory annual livestock anthrax vaccination. Our objective was to assess how the epidemiology of human anthrax has evolved from 2000–2013 in Georgia, in the wake of this cessation. We used passive surveillance data on epidemiological surveys of human anthrax case patients. Risk factors and rates of self-reported sources of infection were compared, before and after the change in livestock vaccination policy. We mapped ethnicity-adjusted incidence during the two periods and assessed changes in the spatial pattern of risk. The overall risk of human anthrax increased >5-fold, from 0.7 cases per 100,000 in 2000 to 3.7 cases per 100,000 by 2013. Ethnic disparities in risk became pronounced; from 2000 to 2013, incidence increased >60-fold in Azerbaijanis from 0.35 to 21.1 cases/100,000 Azerbaijanis compared to 0.61 to 1.9 cases/100,000 among ethnic Georgians. Food-borne exposures from purchasing meat increased from 11% in 2000–2006 to 21% in 2007–2013. Spatial analyses revealed a shift from a random pattern of reporting pre-policy change to clustering among district municipalities following the change in policy. Our findings indicate there were unintended human health consequences associated with changing livestock vaccination policy. Following a reduction in the immunizations administered, there was a major shift in the epidemiology of human anthrax in Georgia. Current infection risk is now highest among ethnic minorities. Increased reporting among individuals uncharacteristically at risk for anthrax from foodborne exposures suggests spillover from modes of agricultural production. Given the importance of human-livestock health linkages, careful evaluations of policy need to be undertaken before changes to animal vaccination are made.

1. Introduction

Anthrax is a zoonotic disease that is found on nearly every continent (except Antarctica) [1,2]. The causative agent, *Bacillus anthracis*, is a soil-borne Gram-positive bacterium with the remarkable ability to survive in the environment for long periods of time, perhaps years, and infect a wide range of hosts [2,3]. Herbivorous animals are most often infected [2–4]. Human infections are typically a result of contact with infected animals or their by-products (e.g. meat or hides) during activities such as livestock slaughtering [1,4].

Targeting livestock with annual vaccination is the most effective method to control anthrax in both humans and animals in endemic regions [1,5]. The most widely used vaccine is the live attenuated Sterne strain (34F2) [5]. In the former Soviet Union (FSU), livestock anthrax vaccination combined with improvements in occupational safety produced a nearly 10-fold reduction in animal cases with a concomitant decline in human incidence [6]. Similar decreases were observed in Europe and the United States following mass vaccination of livestock [7]. However, despite the effectiveness of vaccination, anthrax persists in areas with weakened health infrastructures and long-term vaccination strategies may be needed in endemic areas [1,8]. Countries of the FSU, sub-Saharan Africa, and southeast Asia have (re)emerged as foci for transmission [9].

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The country of Georgia has experienced repeated outbreaks of human anthrax with a recent increase in human incidence (2010–2012) [10]. Reports of an anthrax-like disease in humans dates to the 17th century [11] and >500 locations have been registered as foci (permanent locations of anthrax risk) in Georgia since 1881 [12]. During Soviet governance, anthrax was a mandatory reportable infectious disease in both humans and livestock. Following the dissolution of the Soviet Union in 1991, and Georgian independence in December of the same year, anthrax reporting remained mandatory. To combat the spread of anthrax, from 1995 through 2006, the government carried out annual compulsory livestock vaccination. In 2007, Georgia ended this policy, placing the responsibility of vaccination on private livestock owners [13].

Yet, little is known about how the alteration in livestock immunization policy and the concomitant decline in the number of anthrax vaccine doses administered affected the epidemiology of human anthrax. In the context of >90% private livestock ownership in Georgia, and the high risk associated with agricultural production, identifying changes in anthrax epidemiology are crucial for implementing control strategies and limiting its spread. Our objective was to assess how the change in livestock vaccination policy impacted the epidemiologic characteristics of human anthrax in Georgia from 2000–2013 by identifying changes in risk factors and rates of self-reported sources of infection.

2. Methods

We obtained passive surveillance data on epidemiological surveys of human anthrax case patients and the annual number of livestock vaccine doses administered from the National Centers for Disease Control and Public Health (NCDC) during 2000–2013. We estimated national incidence rates per 100,000, using population data from the Georgian national census (Georgian State Statistical Committee, GeoStat). To describe the trend in human anthrax incidence and identify trend breakpoints if present, we used segmented regression (JoinPoint 4.4.0.0, https://surveillance.cancer.gov/joinpoint/) [14]. Breakpoints in a trend are characterized by an inflection point in the line segment indicating an increasing or decreasing rate of change [14]. We defined the dependent variable as the annual crude incidence rate and independent variable was the year. To adjust for heteroscedastic errors, we used a weighted least squares approach with weights applied to each observation [14]. We allowed for between 0 and 2 breakpoints in the regression line. For each possible regression line segment provided by the best fit model, the rate of change is given by the average annual percent change (AAPC).

Risk ratios and incidences per 1 million were estimated for age, sex, ethnicity, region, self-reported source of exposure, season, and occupation. Season was defined as: winter (December January, and February); spring (March, April, and May); summer (June, July, and August); fall (September, October, and November). We derived a binary dummy variable for each region with ethnic enclaves defined as district municipalities with $\geq$30% of the population reporting as non-Georgian. Statistical analyses (Fig. S1) and accompanying 95% confidence intervals of estimates were performed in R v3.3.1 (R Core Development Team).

Human anthrax data were aggregated to district municipality, and we mapped crude average annual human incidence per 100,000 persons (total cases/population) for each district during 2000–2006 and 2007–2013. The ethnic composition (percent of non-Georgian population) of each district was derived from the Georgian census (http://www.geostat.ge/).

We used classifications of four main ethnic groups defined in the census data: Georgian, Azerbaijani, Armenian, and other (Russian, Ukrainian, Greek, and Yazidi). We calculated ethnicity adjusted incidence rates per municipality before and after the policy change using the indirect standardization method with an internal standard, a best practice in age- or ethnicity-adjusted spatial analyses [15,16].

To test for changes in the spatial dependence in human anthrax incidence among district municipalities between the two time periods, we used the global Moran's *I* statistic (OpenGeoDa 1.0.1, GeoDa Center, ASU, Arizona). This statistic is a measure of spatial autocorrelation or similarity among spatial units with values close to +1.0 indicating clustering and values close to −1.0 indicating dispersion [17]. To characterize the spatial relationship among district municipalities, we used a queen contiguity matrix with row standardization [18]. We tested the null hypothesis of no spatial association in incidence rates of human anthrax among district municipalities before and after the change in policy for both crude and ethnicity adjusted rates.

3. Results

3.1. Temporal trends

From 2000 to 2013, 736 human anthrax cases (annual range: 15–143) were reported in Georgia (Fig. 1). During this 14-year period, the trend in rates was characterized by a breakpoint in the regression line in the year 2010 (95% CI: 2008, 2011) indicating an increasing rate of reporting post-policy change with an AAPC = 10.2% (95% CI: 9.3, 10.9; p = .02) (Fig. 1). The annual human incidence per 100,000 increased from 0.6 cases (95% CI: 0.4, 0.8) in 2000 to 3.7 cases (95% CI: 3.1, 4.4) in 2013. Following the policy change in 2007, there was a precipitous decline in the average annual number of livestock anthrax vaccine doses administered: 2 million (95% CI: 1.2, 2.8) doses were administered during 2000–2006 compared to 201 thousand (95% CI: 32, 436) doses during 2007–2013 (Fig. 1).

Persons age 40–64 years had higher rates of human anthrax nearly every year except in 2010 when they were surpassed by rates in persons age 65 years and older (Fig. 2). Prior to 2007, annual incidence rates were not consistently higher among any ethnic group. In 2007, when the compulsory livestock vaccination program supported by the government ended, incidence rates increased among all ethnic groups (Georgians, Azerbaijanis, and Armenians). Rates began to diverge in 2010 with a rapid increase in the risk of human anthrax among ethnic Azerbaijanis; rates among ethnic Azerbaijanis ranged from 0 to 25.3 cases per 100,000 (Fig. 3).

3.2. Risk before and after policy change

When comparing time periods before and after the policy change, males were two times more likely to have reported human anthrax compared to females during 2000–2006; by 2007–2013 males were at least four times more likely to have reported compared to females (Table 1). Persons age 40–64 were at higher risk of infection compared to all other age groups during 2000–2006 and remained so following the policy change. From 2000–2006, Azerbaijanis accounted for 8% of cases, increasing to 30% during 2007–2013; the relative risk compared to Georgians increased from 1.3 to 6.1 (Table 1). Azerbaijanis and Armenian ethnicities comprised approximately 8% of the total Georgia population while accounting for 35% (187) of all anthrax cases during 2007–2013. Notably during 2012–13, these ethnicities accounted for 48% of all cases (Fig. 3). Regionally, ethnic enclaves were two and a half times more likely to report anthrax cases compared to other district municipalities prior to the policy change, increasing to six